

Anthrax

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Anthrax

Summary

- Anthrax is caused by a large Gram-positive bacterium, *Bacillus anthracis*
- Bacterium can survive adverse environmental conditions as a resistant spore
- Can be used as a biological weapon
- There is no human-to-human transmission
- Pathology caused by powerful exotoxins
- Cutaneous anthrax: skin ulcers with oedema
- Respiratory anthrax: fulminant mediastinitis / pneumonia, meningitis, septicaemia
- Treatment with penicillin, ciprofloxacin, rifampicin, clindamycin
- Neutralisation toxin with antitoxin, e.g. raxibacumab or analogues

General

Anthrax is a widespread zoonotic infectious disease caused by a **large Gram-positive rod-shaped** bacterium: *Bacillus anthracis*. Anthrax is usually a disease of **herbivores**. The animals are infected by grazing in an area contaminated with bacterial spores. Mortality in these animals is high and the carcasses will in turn contaminate the soil. This animal disease also affects man. People die not so much from the invasion of this pathogen but from the **toxins** that are secreted.

The causative agent of anthrax was identified by French biologist Casimir-Joseph Davaine in 1863 and by German bacteriologist Robert Koch, who isolated the organism in pure culture in 1876.

Toxin

The bacterium is surrounded by a polypeptide capsule (polyglutamic acid) that protects the pathogen against phagocytosis. As in other toxin-dependent diseases caused by Gram-positive bacteria such as tetanus or diphtheria, the pathogenesis of anthrax is attributable in the first place to **exotoxins** that are produced. Strains that cannot produce toxins are avirulent. The principal virulence factors of *B. anthracis* are coded on two **plasmids**; one involved in the synthesis of the capsule and the other coding the exotoxins.

The vegetative pathogen releases toxins that have a complex action. The exotoxins are binary and consist of a **B (binding) protein that is necessary for cell penetration** and an **A (active)**

protein that causes metabolic dysfunction. There are three proteins: PA (protective antigen), LF (lethal factor) and EF (oedema factor).

LF is a zinc metalloprotease which kills cells by proteolytic cleavage of several members of the MAP kinase signal transduction pathway. EF is a calmodulin-dependent adenylate cyclase which catalyses the conversion of ATP to cAMP, causing an elevation in cAMP levels. This leads to pronounced oedema, inhibition of neutrophils and monocytes.

Anthrax spores

In certain circumstances *B. anthracis* can form an **endospore**. Spores like this are **very resistant to unfavourable environmental conditions**. The pathogen survives as a spore in the soil for many years, but seemingly less easily in acid soil than neutral soil.

Anthrax spore survival

This long survival was shown very clearly by experiments in the Second World War when Gruinard Island to the north-west of Scotland was deliberately contaminated with the pathogen in order to establish the effects on experimental animals such as sheep. Many years later viable spores of the bacterium were still found in the soil. This required a very aggressive decontamination of the whole of the island in 1986.

In April 1979 there was a notorious accident in Sverdlovsk (now Ekaterinburg) in Russia, in which 66 people died from inhalational anthrax. It is now certain that the cause was an accident in a biological weapons installation of the Russian BioPreparat Programme. About 10 kg of anthrax spores (4 different strains) were released because someone failed to replace a filter on an air vent. People were infected up to a distance of 4 km away from the installation. There were even cases in animals 50 km further away. All the cases occurred in a period of 6 weeks after the incident.

In the period 1979-80 there was an epizootic among cattle in Zimbabwe with about 10,000 infections (epizootic = “epidemic in animals”). Human cases were generally limited to cutaneous anthrax.

Clinical aspects

Cutaneous anthrax

If someone has contact with animal fur or skin in which there are anthrax bacteria, the skin can become infected. Infection can also follow a bite by an infected horsefly (mechanical transmission of the pathogen).

After a **short incubation period of 2 to 3 days**, a **small red skin wheal** occurs at the inoculation site. This can itch at first. Over the course of the next week vesicles form around the central lesion. Occasionally there are atypical cases without vesicles. A central painless ulceration follows. The ulcer is dry, with minimal or no pus. There is often a black crust, hence the name “anthrax” = charcoal. The ulcer is surrounded by red gelatinous local oedema, which sometimes becomes massive (e.g. lesions in the face / neck). Regional lymphadenopathy with lymphangitis and moderate fever can occur, but often the patient is afebrile. The pathogens can multiply in the lymph nodes. The regional lymph nodes are often painful. Superinfection by pyogenic pathogens is rare. There is no peripheral leucocytosis. The skin lesion heals slowly (2-6 weeks) in more than 90% of cases but in rarely there is progression of the infection, with systemic involvement. Without antibiotics mortality can be as high as 20 percent.